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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/656,034	09/05/2003	James Hunter Boone	TLAB.100294	8482

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EXAMINER	
VENCI, DAVID J	
ART UNIT	**PAPER NUMBER**
1641	

MAIL DATE	DELIVERY MODE
10/04/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/656,034	BOONE ET AL.	
	Examiner	Art Unit	
	David J. Venci	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *July 26, 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,7-14,17,18 and 21-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,7-14,17,18 and 21-24* is/are rejected.

7)☒ Claim(s) *2,3 and 12* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 26, 2007, has been entered.

Claims 1-3, 7-14, 17, 18 and 21-24 are pending and under examination.

Claim Objections

Claims 2, 3 and 12 are objected to under 37 CFR 1.75(c), for being in improper dependent form for failing to further limit the subject matter of base claims 1 and 11. Claims 2, 3 and 12 do not appear to further limit base claims 1 and 11 because base claims 1 and 11 already recite a step of indicating ulcerative colitis.

Applicants are required to cancel the claims, amend the claims into proper dependent form, or rewrite the claims in independent form.

Claim Rejections - 35 USC § 101

Section 101 of 35 U.S.C. reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-3, 7-14, 17, 18 and 21-24 are rejected under 35 U.S.C. 101 because the claimed invention lacks credible[1] utility.

Independent claim 1 recites a method for "differentiating between ulcerative colitis and Crohn's disease". Independent claim 11 recites a "diagnositic assay for differentiating between ulcerative colitis and Crohn's disease". Independent claim 17 recites a method for "screening for ulcerative colitis". All of claims 1, 11 and 17 are based on a determination of anti-neutrophil cytoplasmic antibodies ("ANCA") in feces.

Applicants' specification posits that testing fecal samples for ANCA is specifically useful for "an indicator of ulcerative colitis", "differentiating between ulcerative colitis and Crohn's disease (see Specification, paragraph [0014], first sentence), and "differentially diagnosing ulcerative colitis from... Irritable Bowel Syndrome" (see Specification, paragraph [0009]).

Applicants' assertion of utility is based on data obtained from a clinical study involving patients presenting with "Crohn's Disease" and "ulcerative colitis"[2] and/or "irritable bowel syndrome"[3] (see Specification, paragraph [0017] *et seq.*). In the clinical study, Applicants used standard immunoassay techniques to determine whether fecal samples from patients possessed ANCA.

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[1] According to M.P.E.P. 2107.02, Office determination of the credibility of Applicants' assertion of utility is based on whether the facts upon which Applicants' assertion is based are inconsistent with the logic underlying Applicants' assertion. In other words, credibility refers to the reliability of Applicants' assertion of utility in view of the logic and facts that Applicants offer to support Applicants' assertion of utility.

[2] Crohn's Disease and ulcerative colitis belong to a disease class called Inflammatory Bowel Diseases (IBD). See MeSH Database, Inflammatory Bowel Diseases, *available at* <http://www.ncbi.nlm.gov>.

Applicants' asserted utility is not credible because the specification does not support the claimed utility. According to Table 4 of Applicant's specification, ANCA is present in only 41% of patients presenting with ulcerative colitis, and only 9% of patients presenting with Crohn's disease (*i.e.*, ANCA is a useful indicator of ulcerative colitis or Crohn's disease in only 41% or 9% of patients, respectively).[4] Therefore, based on the data in Table 4, it appears that ANCA is not specifically useful as "an indicator" of either ulcerative colitis or Crohn's disease. Necessarily, ANCA cannot be specifically useful for "differentiating between ulcerative colitis and Crohn's disease".

In addition, the prior art does not support the claimed utility. For example, Ferguson *et al.*, 99 CLIN. EXP. IMMUNOL. 70 (1995), found no statistically significant difference in fecal IgA concentration between patients with ulcerative colitis versus Crohn's disease (see Fig. 1, bottom left panel, comparing □ versus ○) and found apparent elevations in fecal IgA are not necessarily specific to either ulcerative colitis or Crohn's disease states (see Fig. 4, observing elevated anti-OVA antibodies in ulcerative colitis and Crohn's disease patients). O'Mahony *et al.*, 31 GUT 1341 (1990), found fluctuations in fecal antibody levels depend on the consistency of the feces before sampling (*i.e.*, whether the feces are initially in semi-liquid or liquid form), which confounds attempts to distinguish between disease states (see p. 1344, left column, first full paragraph), even after normalizing sample dilution to a colostral IgA standard (see p. 1342, paragraph bridging left and right columns, "the IgA content of any given sample was determined by taking the mean IgA content of those two sample dilutions whose optical density fell within the range of the standard curve").

Thus, even in light of the prior art, the instant specification does not support a credible utility.

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[3] Applicants' specification does not disclose what standard, if any, Applicants used to identify and include a patient as having "irritable bowel syndrome" into the clinical study.

[4] Although Applicants' specification discloses a method having 92% specificity, Examiner posits that, in the instant application, this statistic may be statistically insignificant due to the existence of selection bias (*i.e.*, bias that arises when individuals included in a study are not representative of the target population for the study). Specifically, according to Table 3, the sampled population has a seemingly exaggerated UC prevalence of 82% (*i.e.*, [51 UC patients] divided by [51 UC patients + 11 healthy controls]). See *also*, Armitage & Colton, *Encyclopedia of Biostatistics*, John Wiley & Sons (1998). According to Armitage & Colton, coverage error (*i.e.*, the difference between statistics based on the population defined by the sampling frame and statistics based on the target population) occurs when there is a lack of correspondence between the frame population and the target population.

Claim Rejections - 35 USC § 112 – first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-14, 17, 18 and 21-24 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by a credibly-asserted utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments

In prior Office Action, claims 1-3, 7-14, 17, 18 and 21-24 were rejected under 35 U.S.C. 101 because the claimed invention lacks utility.

In response, Applicants amend independent claims 1, 11 and 17 to now require samples from persons "presenting with inflammatory bowel disease". Applicants argue that despite the mere 41% sensitivity of Applicants' test, Applicants' test is "92% accurate in diagnosing UC (Specificity)".

Applicants' arguments have been carefully considered but are not persuasive.

Applicants' test is **not** 92% accurate in diagnosing UC. Although Applicants' specification discloses a method having 92% specificity, Examiner posits that, in the instant application, this statistic may be statistically insignificant due to the existence of selection bias (*i.e.*, bias that arises when individuals included in a study are not representative of the target population for the study).[5]

[5] *Id.*

Conclusion

No claims are allowable at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Venci whose telephone number is 571-272-2879. The examiner can normally be reached on 08:00 - 16:30 (EST). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

David J Venci
Assistant Examiner
Art Unit 1641

djv

LONG V. LE 09/28/07
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